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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,886	03/30/2001	Martha K. Newell	C1102/7002(HCL)	7558

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EXAMINER	
KALLIS, RUSSELL	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,886	NEWELL ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *1-6,8-24,28-37 and 42-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,25-27,38-41 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Claims 7, 25-27, 38-41, and 49 of Group VIII and SEQ ID NO: 8 in Paper No. 10/06/2003 is acknowledged. The traversal is on the ground(s) that restriction to a single nucleotide sequence is inappropriate. This is not found persuasive because each nucleotide sequence is an independent and patently distinct invention requiring a different search.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-49 are pending. Claims 7, 25-27, 38-41, and 49 are examined. Claims 1-6, 8-24, 28-37, and 42-48 are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-27 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims "UCP expression" and UCP inhibitors for use in methods to regulate UCP expression or reduce UCP expression or activity in a plant.

Applicant describes UCP nucleic acid sequences of SEQ ID NO: 1, 3, 5, and 7-12 isolated from human, *Arabidopsis,* potato, and wheat; nucleotides, nucleotide analogs, tocopherols, and non-omega-3, -6 fatty acids known in the art.

Applicant does not describe UCP binding peptides, UCP antibodies, UCP dominant-negative nucleic acids or UCP encoding nucleic acid sequence other than SEQ ID NO: 1, 3, 5, and 7-12.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.,* 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Based upon the disclosure of SEQ ID NO: 1, 3, 5, and 7-12; nucleotides, nucleotide analogs, tocopherols, and non-omega-3, -6 fatty acids known in the art there is insufficient relevant identifying characteristics to allow one skilled in the art to completely determine the structure of a broad genus of UCP inhibitors, that inhibit UCP expression or activity, absent

further guidance. Since the claimed genus encompasses undisclosed or yet to be discovered inhibitors that inhibit UCP expression or activity, the disclosure of SEQ ID NO: 1, 3, 5, and 7-12; and the nucleotides, nucleotide analogs, tocopherols, and non-omega-3, -6 fatty acids, does not provide adequate description of the claimed genus of UDP inhibitors. In view of the level of knowledge and skill in the art one skilled in the art would not recognize from Applicant's disclosure that Applicant was in possession of the broadly claimed genus of UCP inhibitors.

Given the failure of a UCP inhibitor to be adequately described wherein UCP expression or activity is inhibited in a plant, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-1111.

Clearly the proteins, polynucleotides, nucleotides, and binding peptides and fatty acids have structures that vary greatly and are only defined by a common function. Applicant has not described a common structural feature of the broadly claimed genus of UCP inhibitors that could be correlated with the claimed function of inhibition of UCP expression or activity. See MPEP 2163 and the Revised Written Description Guidelines cited previously, which teach that a demonstration of correlation between a structure and a function is required to adequately describe a broadly claimed genus.

Claims 7, 25-27, 38-41, and 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims methods of regulating fuel metabolism in a plant by regulating UCP expression in a plant cell wall; of decreasing the expression or activity of UCP expression in a plant cell wall, plasma membrane, or chloroplast thereby producing a nutritionally enhanced plant; and preventing infection in a plant by preventing an increase in oxygen free radicals.

Applicant teaches that when comparing UCP expression levels between different strains of *C. reinhardtii*, increased UCP expression levels were directly correlated with decreases in reactive peroxide oxygen species thereby suggesting that UCP functions to prevent increased levels of oxygen free radicals (specification, page 42).

Applicant does not teach any methods of regulating fuel metabolism in a plant, or a method of decreasing UCP expression using any inhibitors of any kind or not, or a method of preventing infection in a plant, or a method for making a nutritionally enhanced plant by reducing UCP expression. Applicant has provided no guidance as to how UCP expression should be regulated, and how such regulation is correlated with regulating fuel metabolism in a plant; and there is no guidance for using any one of the broadly claimed UCP inhibitors. Further, since "regulating" encompasses both increasing and decreasing, decreasing UCP expression or activity would not enable both an increase and a decrease in fuel metabolism.

Applicant has deduced that when comparing UCP expression levels between different strains of *C. reinhardtii*, increased UCP expression levels were directly correlated with decreases in reactive peroxide oxygen species thereby suggesting that UCP functions to prevent increased levels of oxygen free radicals (specification, page 42, lines 6-16).

The specification is not enabling for regulating fuel metabolism in a plant by regulating UCP expression; for a method of producing a nutritionally enhanced plant; or for a method of preventing infection in a plant by decreasing UCP expression or activity because it is well know in the art that oxygen reactive species are toxic to the plant and their role in preventing infection is to destroy areas of infection in a localized fashion. Applicant has provided no guidance for accomplishing any of these methods using the claimed UCP inhibitors. Further, the claimed UCP inhibitors have different mechanisms of action and the disclosure does not provide guidance for using the broadly claimed genus of UCP inhibitors.

Regulating fuel metabolism in a plant is a complex process involving pathways that are subject regulation of activity to maintain homeostasis with their environment. Applicant has provided no working examples for regulating fuel metabolism in a plant. The specification supports redirecting metabolic activity towards thermogenesis on page 9, lines 1-9; but does not teach how this can be achieved using the claimed inhibitors and thus the method is not enabled.

The presence of multiple isoforms of a single UCP gene family when attempting to alter UCP expression or activity using chemical or antisense inhibitors is unpredictable because although many UCP proteins may have a common function they may have different coding sequences and one may escape inhibition by antisense when using the other as the inhibitor. Another unpredictable aspect when attempting to engineer expression or activity in a plant arises when protein isoforms have different regulatory properties wherein one isoform is not responsive to an external stimuli that would inhibit other gene family members. This is demonstrated in the analysis of two UCP proteins in *Arabidopsis* where the two UCP proteins have similar sequence identities but different responses to chilling, suggesting that they would have different responses

to inhibition by means other than chilling (Watanabe A. *et al.* Plant Cell Physiology, 1999, Vol. 40, No. 11; pages 1160-1166; see page 1166 column 2, last paragraph).

Plants having high levels of oxygen reactive species are not considered nutritionally enhanced, but are viewed by one of skill in the art to be compromised with respect to their nutritional value. Applicant has argued on page 10 of the specification that decreasing the activity of UCP in a plant will increase the yield of fat in a plant. It is not clear what Applicant means by fat. Nonetheless, increasing the yield of fat in a plant is not recognized as nutritionally enhanced. Further, Applicant merely recites that decreasing UCP expression or activity in a plant will produce a nutritionally enhanced plant (specification page 4, lines 30-32). Since, the disclosure does not provide guidance for applying any of the claimed inhibitors to achieve this effect, the specification does not provide adequate support for a nutritionally enhanced plant. Moreover, it is generally considered in the art that increasing the number of antioxidant species in a plant will actually increase the nutritional value of a plant. The prior art corroborates this view by teaching that dietary components having antioxidant activity have been associated with reducing the effects of oxygen free radicals (Meydani M. Annals of the New York Academy of Sciences. 2001, April; Vol. 928: pages 226-235; see abstract). Furthermore, Applicant's attention is directed to Claim 49, drawn to preventing infection in a plant by decreasing the expression or activity of UCP in a plant in an amount to prevent an increase in oxygen free radicals to prevent infection in a plant. The specification on page 42, lines 6-16, teaches that increased UCP expression levels were directly correlated with decreases in reactive peroxide oxygen species thereby suggesting that UCP functions to prevent increased levels of oxygen free radicals. Clearly, the specification teaches the opposite of the claims, that a decrease in UCP expression or

activity is correlated with a prevention of an increase in oxygen free radicals, and thus the specification is not enabling for a method of preventing an infection in a plant. The prior art corroborates this view wherein overexpression of UDP in tobacco was a requirement for a reduction of damaging oxygen reactive species (Brandalise M. *et al.* Journal of Bioenergentics and Biomembranes, 2003, Vol. 35, No. 3 pages 203-209; see page 204, last paragraph, col. 1). Clearly both the disclosure and the prior art do not support Applicant's claim that decreasing the UCP expression or activity in a plant will prevent an increase in oxygen free radicals, and hence the disclosure is not enabling for preventing infection in a plant or producing a nutritionally enhanced plant.

See *In re Fisher,* 166 USPQ 18, 24(CCPA 1970) which teaches "That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved."

Given the unpredictability in the art as to regulating plant fuel metabolism or decreasing UCP expression in a plant to enhance nutrition or prevent infection in a plant; the breadth of the claims encompassing the use of a wide range of inhibitors for a variety of methods; the lack of guidance in the examples of the specification or in the prior art as to which inhibitors would best

serve the invention and would decrease UDP activity in a plant; although one of skill in the art can readily apply inhibitors or introduce antisense nucleic acids one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictable eliminated, and thus undue trial and error experimentation would be needed by one skilled in the art to test a multitude of non-exemplified inhibitors in a myriad of non-exemplified plants for regulated UDP expression to regulate fuel metabolism; or to reduce UDP expression or activity to enhance nutrition in a plant or to prevent infection in a plant, and thus alter the phenotype in a multitude of non-exemplified transformed plant species. Therefore, the invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 25-27, 38-41, and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claims 7, 25, 26, 38, 39 and 49, it is not clear if "/" denotes "and", "or", or "and/or".

In Claims 25, 26, 38, 39, and 49, "decreasing the expression or activity of UCP" or "the expression or activity of UCP in the plant cell wall/plasma membrane or chloroplast is decreased" lacks a comparative basis.

In Claim 27, line 2, "such as" is indefinite. It is unclear whether "anti-UCP antibodies" was intended to be a claim limitation.

In Claim 40, "UCP inhibitor" has no antecedent basis in Claim 38.

In Claim 49, lines 3-4, it is not clear if there is any relationship between "prevent an increase in oxygen free radicals" and "prevent infection in a plant".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 25-27, 38- 39, 41, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Kowaltowski A.J. *et al.* FEBS Letters, 1998, Vol. 425; pages 213-216.

Kowaltowski teaches that the activity of UCP was decreased in potato mitochondria upon the addition of ATP and thus the reference teaches the method steps of regulation of UCP expression and decreasing the expression or activity of UCP in a plant cell wall, a plant plasma membrane or a plant chloroplast by contact with a nucleotide inhibitor required for the method of regulating fuel metabolism in a plant, the method of producing a nutritionally enhanced plant and the plant thereof, and the method of preventing an infection in a plant, and thus the reference teaches all the limitations of Claims 7, 25-27, 38-41, and 49.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7, 25-27, 38-41, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kowaltowski A.J. *et al.* FEBS Letters, 1998, Vol. 425; pages 213-216 wherein the choice of

antisense as an inhibitor of UCP activity would have been an obvious design choice because anitsense inhibition is well known in the art.

It would have been obvious at the time of Applicant's invention to modify the invention of Kowaltowski to include an antisense inhibitor. One of skill in the art would have been motivated by the knowledge common in the art that antisense of plant genes are valuable materials for genetic engineering of plants and the success of Kowaltowski in reducing the expression of UCP in a plant, and that one would have had a reasonable expectation of success of expressing antisense genes in transformed plants and plant cells.

All Claims are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

Russell Kallis Ph.D.
December 10, 2003

Phuong Bui 12/12/03

PHUONG T. BUI
PRIMARY EXAMINER